markably persistent pylorospasm may be noted in some cases. At times cardiospasm may be a feature or the entire stomach may contract abnormally and give peculiar outlines on the X-Ray screen or plate (literature given by Buttner, Intermittirender Spasmus der beiden Magenporten als Reflexneurose bei Cholelithiasis Arch. fur Verdauungs krankheiten XVI Heft. 2. Emmo Schlesinger, Totaler Gastrospasmus, rontgenologisch nachgewiesen bei Cholecystitis und cholelithiasis Berliner klin. Woch. 1912 No. 26). There may be gastric atony instead of spasm and hypochlorhydria instead of hyperacidity. Dilatation may follow stenosis of the pylorus or duodenum due to adhesions between gall-bladder and stomach or intestine. Vomiting and retention characteristic of such stenosis and disturbed motility will now direct attention from the original disease unless a good history traces the order of successive symptoms. Free hydrochloric acid is frequently absent in such cases and I have notes of five patients in whom the stomach-content gave the tests usually present in carcinoma, absent free HCl, absent ferments, lactic acid and Boas Oppler bacilli present. In three cases there was a Gram positive intestinal flora. In one of these patients, a man, hematemesis occurred on two occasions, and yet the history, a good appetite and a clean tongue spoke strongly against stomach carcinoma. The operation showed a gall bladder filled with stones adherent to the duodenum. In a stout woman seen recently in the course of a very severe biliary colic of two days' duration—so severe as to suggest a pancreatic complication—the attack was attended with the passage of a considerable amount of dark blood from the bowel. A nurse, aged 35, who had had typhoid at 25 had symptoms of gall-bladder disease for eight years. At first there was dyspepsia with occasional epigastric pain, later pain in the right hypochondrium with the appearance of a distinct tumor during severe attacks. During the last two years of illness there had been continued stomach distress with frequent vomiting and evidence of retention. Attacks of tetany had occurred in the last year. Operation disclosed a a large gall-bladder with stones and adhesions to the duodenum and stomach dilatation.

Involvement of the pancreas is much more common in connection with bile-duct than with gall-bladder disease. Glycosuria is occasionally seen in gall-bladder affections without pancreatic complications. Extreme pain, collapse, cyanosis, symptoms of ileus are more common when acute pancreatitis complicates gall-bladder or gall-duct disease. Chronic pancreatitis may lead to emaciation, persistent jaundice and a palpable abdominal tumor.

In a few patients cardiac insufficiency seems directly referable to chronic gall-bladder infection; Babcock of Chicago has written of the frequent connection. Riesman has noted the frequency of mitral systolic murmurs in biliary colic and has suggested that the sign may help in the differentiation from renal colic or appendix pain.

CHOLELITHIASIS WITH A SHORT REVIEW OF ONE HUNDRED NECROPSIES.*

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Cholelithiasis is a very common disease. Our one hundred cases occurred among 1648 necropsies or expressed in percentage in 6% of all necropsies including infants, children, men and women. Higher percentages up to 15% have been reported from other places.

Our material also shows a relative preponderance of the disease in women, although the actual number of cases observed among men is larger, but this is due to the fact that many more males were examined than females.

We did not find one instance of cholelithiasis in a person below 30 years of age and the largest number of cases occurred between 40 and 60 years of age, which corresponds well with statistics published elsewhere. It is a well known fact that gall stones are very rare in children, although a few cases have been reported in childhood and even in early infancy. Still,[1] for instance, found eleven bilirubin stones in an infant of nine months and three calculi in another infant eight months of age. On account of the frequently long period of latency of the disease and on account of the large preponderance of old people who come to autopsy it would seem probable that as a rule gall stones develop rather earlier in life than would appear from such statistics.

It is impossible to enter into a minute description of the various forms of gall stones. Their appearance is familiar to all of you. They vary from just visible to stones of the size of a hen's egg and larger, and in consistence they may be all the way from soft, either pasty or grumous, to hard calcareous masses, which are difficult to cut with the knife.

It is more important to distinguish different varieties of gall stones, although it must be confessed that the classification of them is by no means easy and obvious in all cases. Roughly we can distinguish between cholestearin stones on the one hand and bilirubin stones on the other, although cholestearin stones usually contain some bilirubin, and vice versa.

The bilirubin is never precipitated as such but always with a certain amount of calcareous material, the amount of which, however, varies considerably, causing the precipitations to be either soft and pasty or of stony hardness. On this account such concretions are also frequently spoken of as pigment lime stones. They are usually small stones of about the size of a birdseed which, according to Boysen,[2] show a very peculiar and characteristic structure in sections produced by grinding, from which the coloring matter has

* Read before the Forty-third Annual Meeting of the Medical Society, State of California, Oakland, April, 1913.

1 Still. Gall stones in children. Pathol. Society of London, 1899.

2 Boysen. Über die Struktur und die Pathogenese der Gallensteine. Berlin, S. Karger, 1909. The Danish original appeared in 1900.

been removed with acids and chlorine. They then exhibit a hyaline clear peripheral layer and an irregular cavity in the center. Larger stones of this variety are formed by fusion of these small units and therefore look somewhat like "mulberries." It is commonly assumed that the smaller stones of this kind often form in the intrahepatic bile ducts and may then be transported into the gall bladder, where they grow into larger stones by accretion or by becoming the nucleus for the formation of ordinary cholestearin stones. Boysen is particularly insistent on this latter point and claims to have found frequently still recognizable remnants of small bilirubin stones in the centers of large cholestearin stones, and he also believes that the more irregular masses of pigment lime which almost invariably form the nucleus of the ordinary cholestearin stones are disintegrated remnants of such bilirubin stones. The importance of these assertions lies in the fact, that it would place the origin of the gall stones in the bile ducts and not in the gall bladder where they are most commonly found, and that the problem of the etiology of gall stones would then be intimately connected with the origin of these bilirubin stones.

The cholestearin stones are much more common and better known. They practically always occur primarily in the gall bladder. They are usually quite numerous and sometimes extremely so, over a thousand having been found in one gall bladder. When present in large numbers they are more or less facetted. When there are only a few of them, they are rounded and the large solitary stones of this kind often are pear-shaped like the gall bladder which contains them. We are all familiar with their main characteristics, their light specific gravity, their peculiar consistence, like a dry somewhat brittle paste, and their pretty crystalline cut surface, which usually shows as well radial as concentric markings. The latter evidently result from the fact that they usually form in consecutive layers. The radial markings are due to the arrangement of the cholestearin.

Our modern conception of the etiology of gall stones appears in many ways well founded and extremely satisfactory. It commenced with the careful researches of Meckel von Hemsbach [3] in the middle of the last century who, from his study of gall stones, came to the conclusion that the formation of a soft organic matrix which he believed he could identify as mucus, was the important factor in their formation and the deposition in it of the solids, like pigment lime or cholestearin, only of secondary importance. This "mucus" which later investigation found to be a proteid material not related to mucus, was furnished by the *"lithogenous catarrh"* of the walls of the biliary tract. The question then naturally arose, whence comes this lithogenous catarrh? The answer was furnished by the work of Gilbert [4] and his pupils in France and by Naunyn [5] in Germany. They asserted that the catarrhal inflammation results from bacterial infection. Gilbert and Fournier showed that in a considerable proportion of cases living bacteria or dead remnants of such could be found not only in the bile in cases of cholelithiasis, but in the very centers of gall stones; the ones most frequently encountered being the bacillus coli communis and the bacillus typhosus. These findings have been confirmed later quite extensively, more especially in our own country. Gilbert crowned his work by succeeding, after many unsuccessful efforts, in producing gall stones experimentally by infecting the gall bladder of animals with certain cultures of colon bacilli or those of the bacillus typhosus. Almost simultaneously Mignot [6] published a very extensive and thorough piece of research in this direction also with many positive results. According to Mignot the success of the experiment does not depend on the species of the infectious agent but on the degree of its virulence, a large number of organisms of a certain low degree of virulence provoking the mild inflammatory reaction of the mucous membrane which leads to formation of gall stones. These views of Mignot's were later confirmed by other investigators, among them by Dr. Lartigau [7] of San Francisco.

Stagnation of bile and subsequent infection of it with colon bacilli or typhoid bacilli or other bacteria of a certain degree of virulence are therefore generally looked upon as the essential cause of cholelithiasis.

The great frequency of the disease in women is usually referred to interference with the flow of bile by tight lacing or by pregnancies, still one may reasonably doubt whether these or similar mechanical conditions are the real reasons.

Those who believe with Boysen that the majority of gall stones commence as small concretions of pigment lime in the bile ducts are not so well satisfied with the infectious theory. They also insist that there must be a catarrhal condition to furnish the organic matrix, but they doubt whether it is necessarily of bacterial origin in all cases.

Aschoff and Bacmeister [8] have recently published a very interesting monograph on cholelithiasis in which they assert that single pure cholestearin calculi may be formed without any inflammation of the bile passages, in fact Aschoff believes that frequently, if not always, the first stone in the gall bladder develops in this way and that only after this stone has caused a certain amount of obstruction and stagnation, bacterial action comes into play and then leads to the formation of the ordinary facetted mixed stones.

The modern conception as initiated by Meckel and more especially as elaborated by Gilbert and Naunyn stamps the disease as a purely local disorder, in strong opposition of the formerly more current view that disturbances in metabolism leading to the oversaturation of the secretions with certain bodies might play some role in the produc-

3 Meckel von Hemsbach. Mikrogeologie. Berlin, 1856.
4 Gilbert & Dominici. La lithiase biliaire est-elle de nature microbienne? Compt. rend de la Soc. de Biol. 1894, 10 s. I, 485 and several preceding and later publications.
5 Naunyn. Klinik der Cholelithiasis. F. C. W. Vogel, Leipzig, 1892.
6 Mignot. L'origine microbienne des calculs biliaires. Arch. gen. de med., 1898, II, 129.263.
7 Lartigau. Relation of bacteria to the development of gall stones. Cal. State Journal of Medicine, 1906. IV. 17.
8 Aschoff and Bacmeister. Die Cholelithiasis. 1909.

tion of calculi, wherever they may be found. What has puzzled me in regard to gall stones is the fact that they undoubtedly occur more commonly in stout persons. Of our one hundred cases one-third were definitely described as either unusually well nourished or as definitely stout, which is a very high average, when we consider, how extremely emaciated many of the patients get to be in the course of the disease; in fact, the loose skin of many of the latter still bore witness to the former affluence of their adipose tissue.

I am therefore of the opinion that certain problems connected with the etiology of cholelithiasis are still awaiting their final solution.

One of the most striking facts about cholelithiasis, corroborated by our series, is the frequency with which gall stones are found at autopsy unassociated with any evidence of consecutive disturbance. Among our one hundred cases there are forty-seven in which gall-bladder, ducts, liver and pancreas were free from all lesions which might be referred to the presence of gall stones. Liver and pancreas were examined microscopically in all cases.

The most common lesion found otherwise is a chronic either diffuse or more localized cholecystitis which may lead to shrinkage and adhesions. The mucous membrane is either intact or often shows a peculiar proliferation of its crypts with deep penetration of the muscular coat, which is well known to pathologists. In other cases the inner surface is ulcerated. In our series there were superficial ulcers in two cases, deep ulcers with perforation in eleven cases. These perforations had led to the formation of abscesses in the adjoining part of the liver or in adhesions around the gall bladder in three cases. I remember especially well one case of cholelithiasis with streptococcus infection with a large abscess of the size of a fist in the liver which freely communicated with the much distended and extensively ulcerated gall bladder. Both abscess and gall bladder appeared to be filled with large blood clots which, on microscopic examination however, proved to be a coagulated hemorrhagic exudate.

These perforations often lead to the formation of false diverticula tightly enclosed in which the gall stones are then found, long after the attack has subsided. We have seen altogether five cases of this character.

If the infection extends into the space between diaphragm and liver, large subphrenic abscesses may develop as in one of our cases.

The discharge of gall stones from the gall bladder either on the body surface or into adjoining hollow viscera by means of such perforations is of course well known. In one of our cases there was such a perforation into the transverse colon, in another into the duodenum, representing the more common occurrences.

The development of hydrops of the gall bladder after occlusion of the cystic duct by gall stones without virulent infection, also seems to be quite frequent. We saw five such cases.

It may not be out of place to remind you at this point, that at operation or autopsy it may be very difficult to decide whether one is dealing with chronic cholecystitis with excessive formation of cicatricial tissue, or with diffuse carcinoma of the gall-bladder. I have seen several such cases which were extremely puzzling in this regard and could not be properly classified until after microscopic examination.

It is somewhat surprising to notice in our series of one hundred cases, that there were only about one dozen in which the stones had arrived in the bile ducts with the usual result of causing obstruction at the papilla, dilatation of the ducts and almost invariably a severe degree of suppurative choleangitis which was associated with multiple abscesses in the liver in three instances. In other cases the long continued infection of the small ducts produced a well marked biliary cirrhosis of the liver, which was observed by us four times.

I am sorry that I cannot enter at length into the very interesting development of our knowledge in regard to the relation of cholelithiasis to pancreatic disease.

A coincidence of the two conditions had been frequently noted ever since pancreatic disease was studied more carefully and the fact that the main duct of the pancreas, the duct of Wirsung, usually opens conjointly with the common duct into the diverticulum of Vater had given further food for reflection, still the interrelation of cholelithiasis on the one hand with such diseases as acute hemorrhagic necrosis of the pancreas and chronic pancreatitis remained quite obscure, until the brilliant researches of Opie [9] threw a flood of light upon the subject. He observed the mechanism through which material in the bile ducts may regurgitate into the pancreatic duct, when the papilla is closed by a small stone, not large enough to fill the diverticulum of Vater and block the pancreatic duct also. In this way a continuous passage is established between the common duct and the duct of Wirsung, if the latter opens in the usual place. He also showed, that injections of a fairly large amount of even normal bile into the pancreatic duct of dogs sufficed to produce acute hemorrhagic necrosis of the pancreas, often associated with disseminated fat necrosis. From later experiments of Flexner [10] it would appear, that the bile salts are the active principle in the production of these pancreatic lesions. It was also determined, that smaller doses of bile are apt to produce more chronic lesions in the pancreas.

Among our cases there were found evidences of chronic pancreatitis in seven instances, in four of which the lesions were quite severe. There were three cases of acute inflammation with recent fat necrosis which in two cases were more circumscribed and in one showed the characteristic appearance of an acute diffuse hemorrhagic necrosis of the pancreas.

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9 Opie. Cholelithiasis and disease of the pancreas. Amer. Jour. of Med. Sciences, 1901, CXXI, 1.
Opie. Etiology of acute haemorrhagic pancreatitis. Johns Hopkins Hosp. Bull., 1901, XII, 182.

10 Flexner. Constituent of the bile causing pancreatitis. Jour. Exp. Med., 1906, VIII, 167.

There were in addition two very interesting cases of old, more or less walled-off fat necrosis. In one of these the cicatricial contraction around a large fat necrosis in the retroperitoneal tissue had led to the obstruction of the superior mesenteric vein with hemorrhagic infiltration and necrosis of a large piece of the small bowel.

In conclusion I may state that entrance of bile in cholelithiasis into the pancreatic duct is not the only cause for such lesions in the pancreas. According to the suggestion of Eppinger [11] and of Polya [12] serious pathological conditions arise in the pancreas whenever there is forced into the pancreatic duct any fluid capable of activating the pancreatic ferments which normally are present in the gland in an inactive state as proferments. The enterokinase of the duodenum would naturally be assumed to play an important role in this direction when its regurgitation into the pancreatic duct which is ordinarily impossible is facilitated by pathological conditions. Opie [13] has made the ingenious suggestion that such may be the case more easily when the pancreatic duct does not open through the duct of Wirsung at the papilla as ordinarily but through the usually atrophic *ductus Santorini* separately from the bile duct with less perfect protection from regurgitation of intestinal contents into it.

[13] Opie. Disease of the pancreas. 2d edition, 1910.

SYMPOSIUM ON GALL-BLADDER.

Discussion.

Dr. Emmet Rixford, San Francisco: There are two or three little points I noted in passing which perhaps might be mentioned. Dr. Moffitt stated that the pain in cholecystitis is due to distension of the gall-bladder; this may be true, but it does not necessarily mean that the gall-bladder under such circumstances is distended, i. e., the gall-bladder may not yield to the distending forces, for it is a common observation of surgeons that the pain is perhaps even greater in those cases of markedly contracted gall-bladder, in which the gall-bladder is little more than a cicatricial sac squeezing down upon the mass of gall-stones.

Dr. Eloesser remarked that the duct of Santorini drained certain portions of the pancreas into the pancreatic duct and that as a safety valve, or means of conducting the pancreatic secretion into the bowel in event of stoppage of the duct of Wirsung, was of little value. However, there is no doubt that it may act as such a safety valve, as shown by the case of a young woman of thirty with carcinoma of the biliary papilla, completely obstructing the ducts (at least it was evident that it produced complete obstruction of the common duct). We removed the carcinoma (November, 1899), implanted the choledochus into the duodenum and ligated the pancreatic duct. The duct of Santorini was exposed in the operation and was preserved. The patient lived for two years without symptoms or evidence of pancreatic indigestion. There were no fatty stools.

Concerning the danger of ascending infection following cholecystenterostomy, I would say that this patient returned one year after the operation with recurrence and in deep jaundice which was relieved by cholecystenterostomy. The operation was done with the Murphy button and no trouble of ascending infection followed, nor did the opening close. In another case of carcinoma of the choledochus in which we performed cholecystenterostomy also with a Murphy button, there was no evidence of ascending infection through many months of observation. We know that the opening did not close by the non-recurrence of the jaundice and by the fact that the Murphy button remained in situ (one objection to the Murphy button).

Dr. Terry spoke of the use of a bolster behind the lumbar region as assisting in exposing the ducts. It does another thing, it makes more tense the anterior abdominal wall. If one flexes the pelvis, doubling the patient up, he will find he can get an excellent exposure and with less difficulty in holding the intestines back and with consequently less trauma.

I am particularly interested in this symposium on gall-stone disease because I think it marks a little change in the Society's attitude toward the subject from that exhibited at Riverside in 1905. At that meeting I read a paper entitled "Early Operation in Gall-stone Disease," and reported 15 cases in my own practice in which there was a history of symptoms which might have been interpreted as indicating the presence of gall-stones. Nearly all these cases had sooner or later serious complications which interfered enormously with attack by operation and which in certain cases made operation futile, e. g., one such patient being opposed to operation had received medical treatment in San Francisco and was finally sent to Carlsbad. The cholecystitis was improved and after a while the patient returned home. On his arrival he had another attack and immediately packed his duds and went again to Carlsbad, with similar improvement. Possibly, had that man spent the remainder of his days in Carlsbad he would have been comfortable for a considerable length of time, but he returned home and shortly thereafter suddenly developed peritonitis. We opened the abdomen and found fat necrosis of the omentum, mesentery and retroperitoneal tissues generally. The digestion by the pancreatic ferments had destroyed the tissues about the mesenteric vein and cicatricial contraction had all but closed the vein. Thrombosis occurred and the man died of necrosis of the entire small intestine and ascending colon.

There were several other cases of chronic pancreatitis with fat necrosis, several of carcinoma in which it is pretty generally agreed that gall-stones are of etiological significance, two cases of perforation of the gall-bladder, several in which adhesions made operation hazardous, one or two cases of phlegmon of the gall-bladder.

I may say that I am very glad to have heard Dr. Terry's paper because I agree with everything he says. His comparison of the attitude of medical men towards early removal of the appendix is precisely the statement I made at Riverside in 1905, and which was earlier made by the late Dr. Richardson of Boston. My paper called forth the remark from a medical gentleman in discussion that 75 per cent. or so of people with gall-stones carry them with little or no discomfort and from a surgeon that "the only reason or justification he could see for advocating early operation in gall-stone disease was the hunger of the surgeon." I am glad to see that the Society is taking a different view of the matter at this time.

I do not, however, wish to put myself on record as advocating indiscriminate operation whenever gall-stones are known or are suspected to be present, and I of course acknowledge the value of medical measures in relieving the symptoms in gall-stone troubles. My position I think was clearly stated in the paper referred to and I have seen no occasion since to modify the opinions there expressed unless to strengthen them, viz., that gall-stones which have caused symptoms warranting the diagnosis to be removed surgically unless there is some complication making operation more

[11] Eppinger. Zur Pathogenese der Pankreasfettnekrose. Zeitschr. f. Exp. Path. & Ther., 1905, II, 216.

[12] Polya. Zur Pathogenese der akuten Pankreasblutung und Pankreasnekrose. Berl. Klin. Woch., 1906, XLIII, 1562.